REMARKS

Reconsideration of the Office Action mailed November 9, 2001, (hereinafter "instant Office Action"), entry of the amendment hereinabove, withdrawal of the rejection of claim 1 and reinstitution of claims 2-88, are respectfully requested.

In the instant Office Action, claims 1-88 are listed as pending, claims 2-88 are listed as withdrawn from consideration and claim 1 is listed as rejected.

Attached hereto as Appendix A is a marked-up version of the changes made to the claims by the current amendment. Appendix A is captioned **"Version With Markings To Show Changes Made"**. Also attached hereto as Appendix B is a complete set of the claims that will be pending upon entry of the amendments presented herein and is captioned **"Pending Claims After Entry Of Amendments"**.

The Examiner has made the restriction requirement final. Applicants respectfully maintain the traversal for the reasons stated in Paper No. 11. Applicants point out that there is no difference between the large genus claims that the USPTO issues every week, which cover a large number of "structurally dissimilar" compounds, and Applicants' instant claim 1, which lists the compounds individually instead of in a genus format (see for example U.S. Patents 6,355,635 and 6,297,238). Applicants are being penalized for form and not on a substantive basis. It can hardly be maintained by the Office that it issues claims only to single pharmacophores. The body of issued chemical patents refute such a stance. Whether the scope of compounds covered in a claim is presented in a genus, an examiner is under a duty to search all permutations of the genus, which is equivalent to searching individually enumerated structures. Therefore, there is no difference between the burden to search Applicants' compounds regardless of how it is presented, i.e., individually or in a genus.

Further, with regard to whether a search is too burdensome, the Examiner's position appears to be too subjective. Again the Examiner implicitly states that searching more than one central molecule is too burdensome. This seems not to be consistent with the searching that had to have been conducted in many other issued U.S. patents, which patents cover a multitude of central molecules.

The Examiner also mentions that "[i]f, say compounds of group I...were anticipated, applicants would not acquiesce in the rejection of elected group 2...thereover or vice versa".

Applicants point out that the relevance of a prior art rejection is always predicated on what the prior art reference teaches or suggests. There is no foregone conclusion that structural similarity is the only basis for a prior art obviousness rejection. Each case must be taken on the merits of the cited prior art and not by a broad brush stroke.

Based upon the foregoing, Applicants respectfully request the Examiner to reconsider the finality of the restriction requirement, and to withdraw the restriction requirement or at the very least to combine compounds of formula 1-117 to a more reasonable number of molecules per group rather than just one per group.

The Examiner has rejected Claim 1 under a judicially created doctrine as being drawn to an improper Markush group. The Examiner suggests that this rejection can be overcome by limiting claim 1 to just the elected group, namely Group 1. Applicants have amended claim 1 as suggested by the Examiner. Therefore, this rejection is obviated and should be withdrawn.

The Examiner has withdrawn claims 2-88 from consideration "because art was found (see M.P.E.P. 803.02)". Applicants respectfully request that claims 2-88 should be reinstated, because claim 1 has been amended so that only the elected Group 1 is covered and, thus, do not claim any non-elected subject matter.

The Examiner has rejected claim 1 under 35 U.S.C. §112, second paragraph, for the reasons stated at page 4 of the instant Office Action. Applicants respectfully traverse this rejection. Applicants response to the Examiner's enumerated points are numbered accordingly to track the Examiner's points.

i) The term "prodrugs" and phrase "biologically active metabolites" are terms of art which are known to one of ordinary skill in the art. The knowledge of what these terms mean is analogous to the level of knowledge by those skilled in the art for the phrase "pharmaceutically acceptable salt". Applicants point out that the Examiner has not questioned what the phrase "pharmaceutically acceptable salt" is probably because the Examiner knows what is covered by the phrase and that there is a common knowledge in the art regarding the phrase. Analogously, the term "prodrugs" and phrase "biologically active metabolites" have a similar level of clarity and definiteness among those skilled in the art. Accordingly, Applicants submit that such terms do not have to be defined in the claims, especially claim 1.

ii) With respect to the term "substituted", Applicants direct the Examiner's attention to page 55, lines 11 to 24, which provides a definition of what is meant by the term "substituted". Applicants submit that the definition of the term " substituted" as is to be read into the claims is clear and definite.

iii) With respect to the term "cycloalkyl", Applicants point out that since the breadth of the term "cycloalkyl" is not limited in any way, and there is no disclosure in the instant application that would cause an uncertain definition of the term, it is clear and definite that the term "cycloalkyl" should be read in its broadest embodiment.

iv) With respect to the term "heterocyclic", Applicants direct the Examiner's attention to page 54, lines 8-25, which defines the term "heterocyclic". Such definition provides a clear and definite understanding of the scope of the term.

Based upon the foregoing, the rejection of claim 1 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

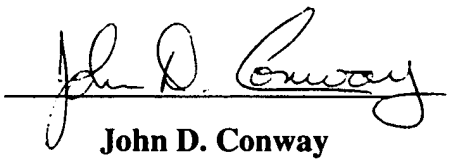
The Examiner has rejected claim 1 as allegedly being unpatentable under 35 U.S.C. §103(a) over Altmann et al. (WO 97/49706). Applicants point out that claim 1 has been amended to only include the elected compound of Group 1, which the Examiner has found to be allowable. Accordingly, the rejection of claim 1 under 35 U.S.C. 103(a) over Altmann et al. is obviated and should be withdrawn.

Based upon the foregoing, Applicants believe that claims 1-88 as amended are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that there are any issues that could be resolved in a telephone conference, Applicants invite the Examiner to call Applicants' undersigned attorney.

Respectfully submitted,

Date: May 9, 2002



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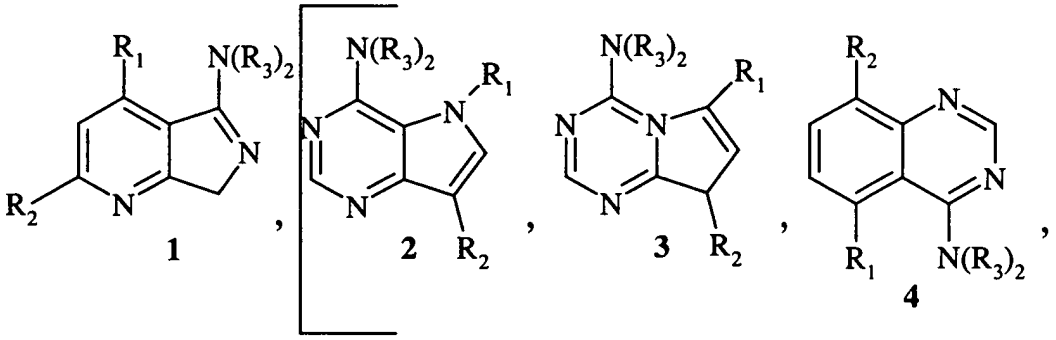
Appendix A

Version With Markings To Show Changes Made

1. (Amended) A compound of Formula (I), the racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof, [selected from the group consisting of]



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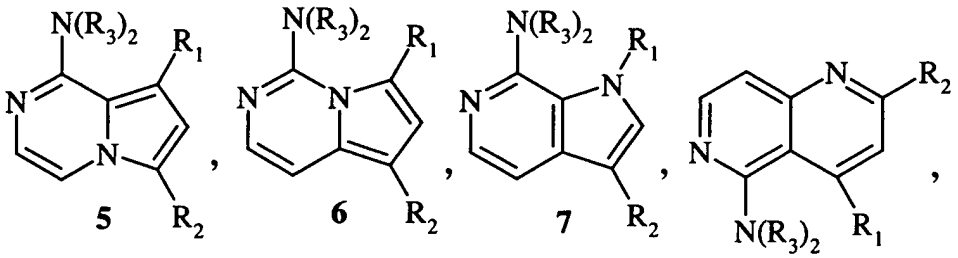

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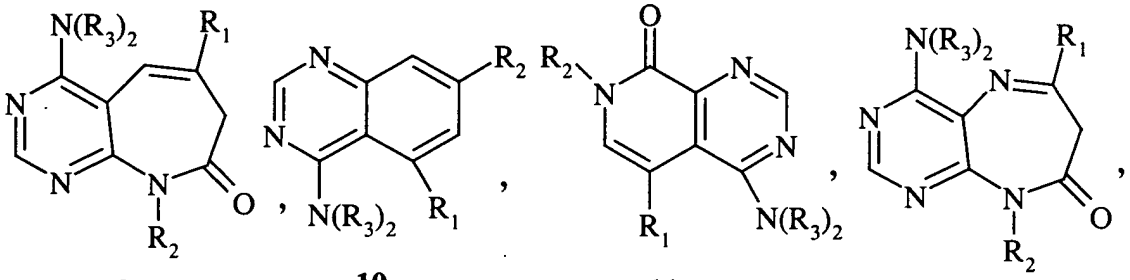

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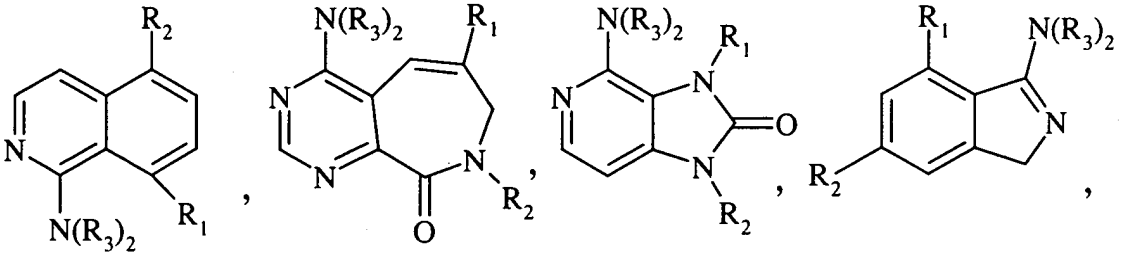

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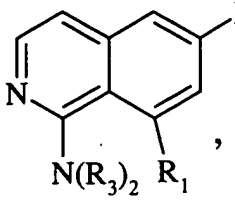

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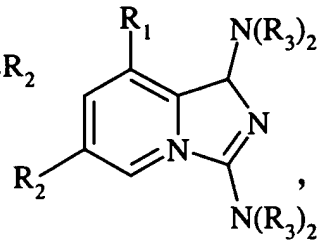

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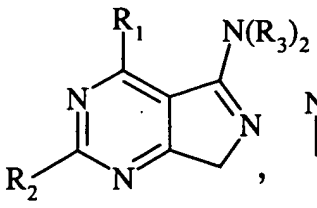

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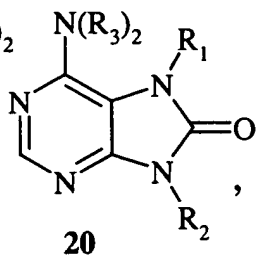

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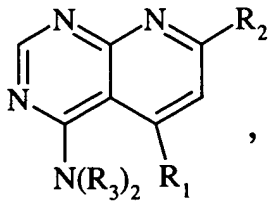

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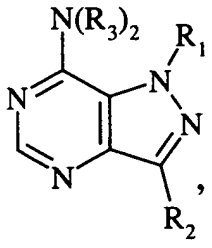

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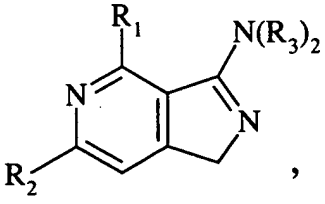

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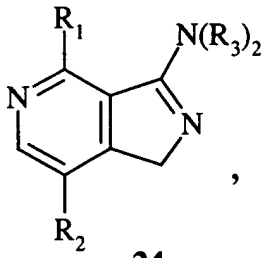

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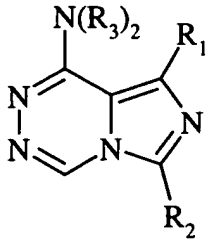

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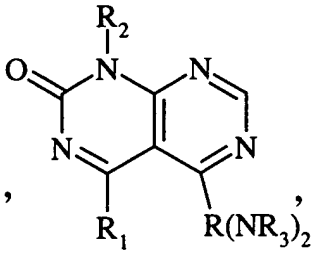

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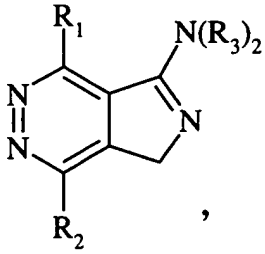

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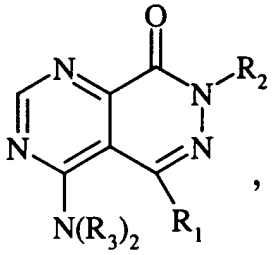

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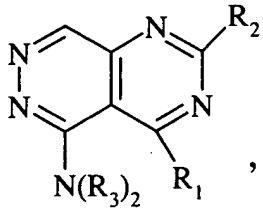

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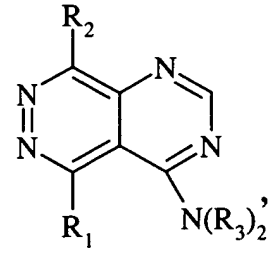

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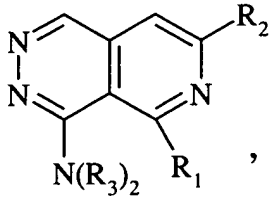

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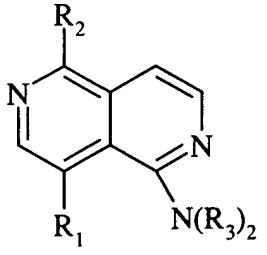

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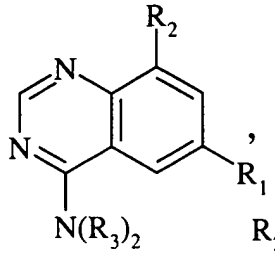

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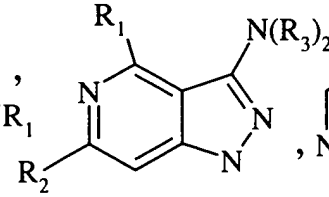

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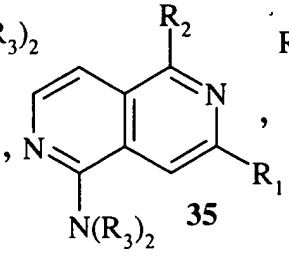

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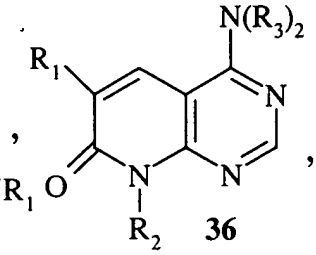

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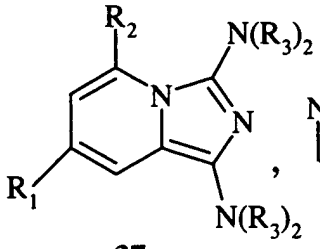

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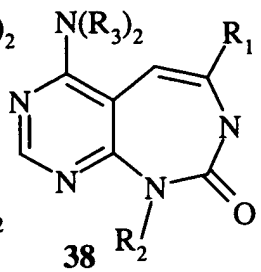

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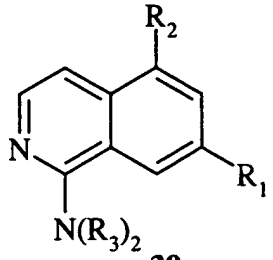

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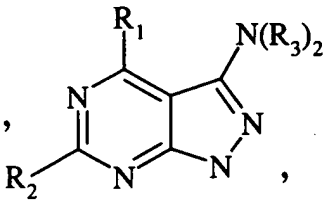

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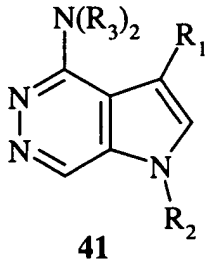

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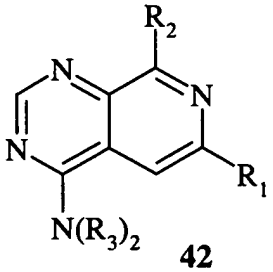

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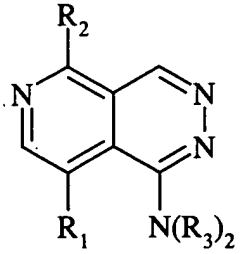

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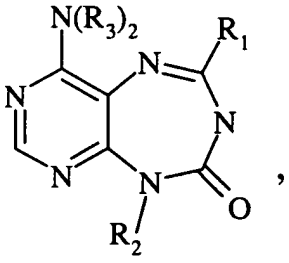

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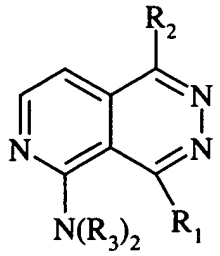

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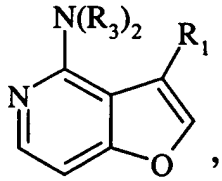

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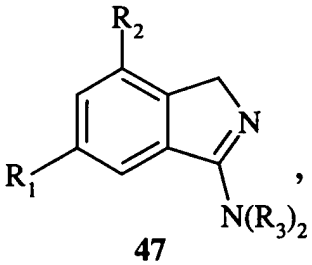

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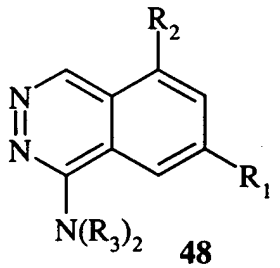

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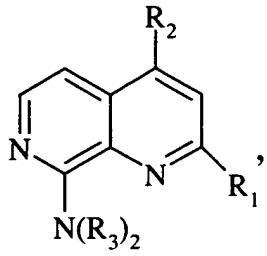

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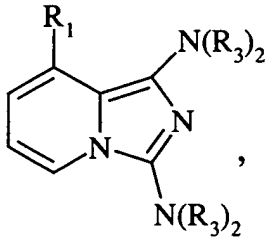

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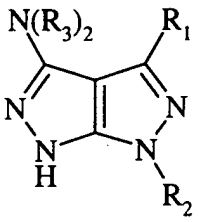

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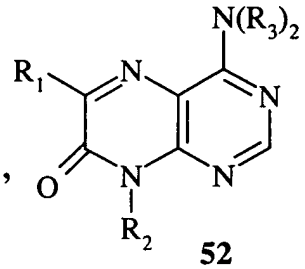

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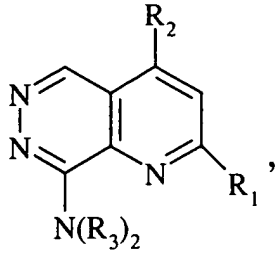

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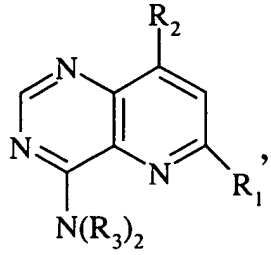

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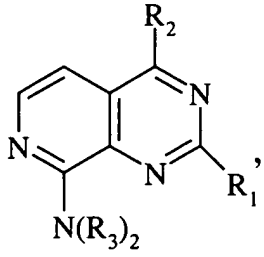

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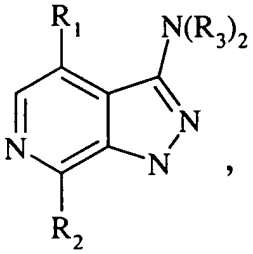

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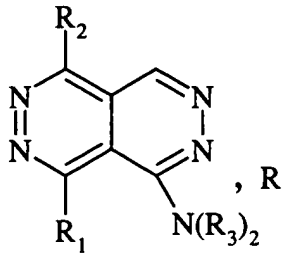

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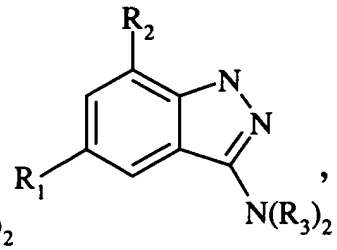

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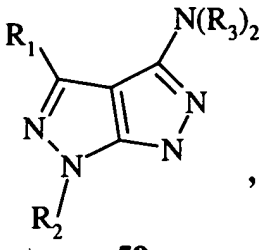

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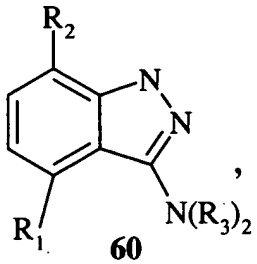

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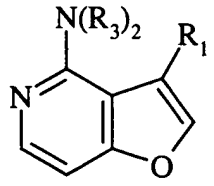

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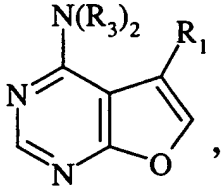

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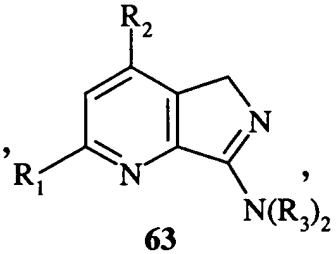

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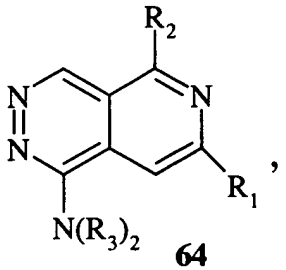

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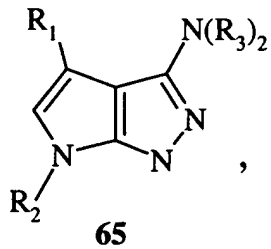

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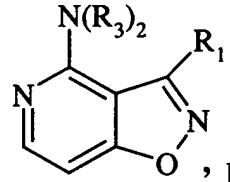

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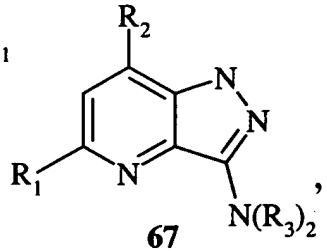

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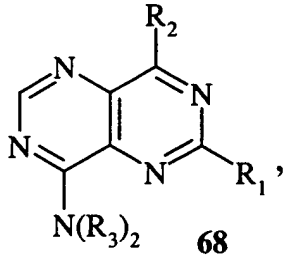

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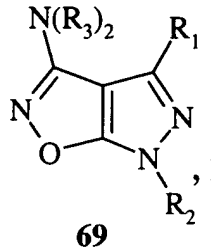

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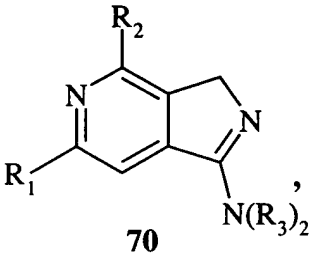

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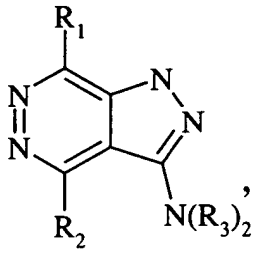

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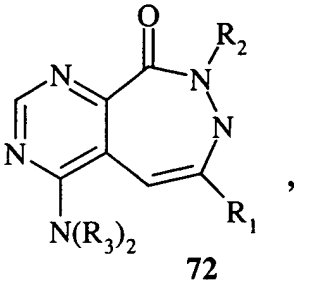

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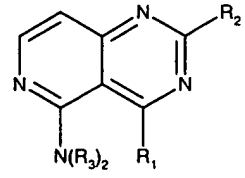

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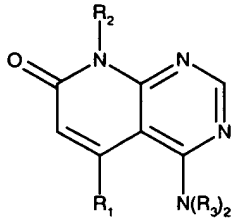

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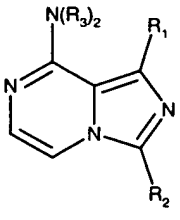

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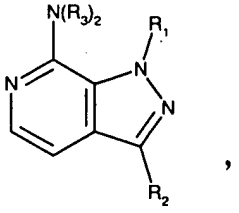

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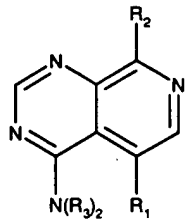

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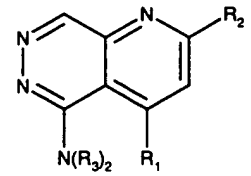

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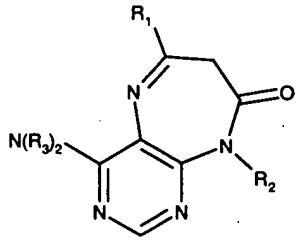

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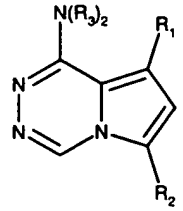

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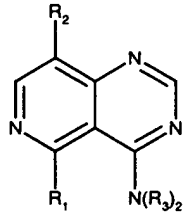

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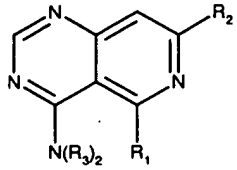

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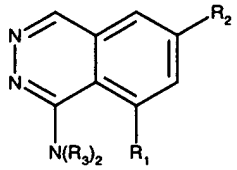

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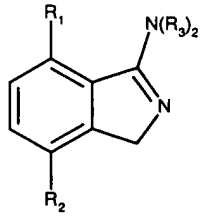

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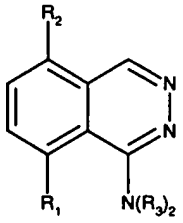

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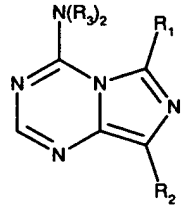

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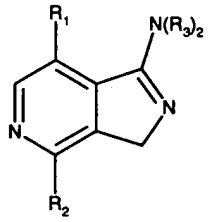

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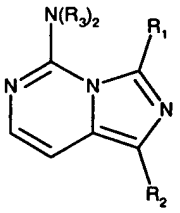

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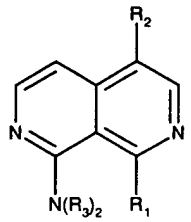

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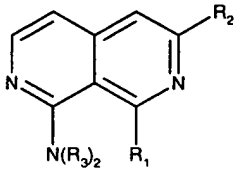

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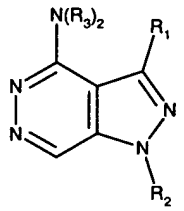

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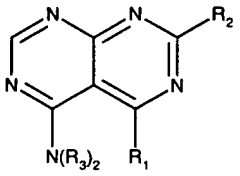

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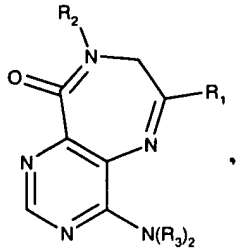

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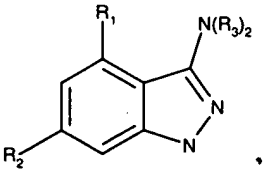

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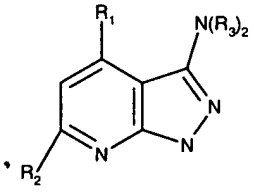

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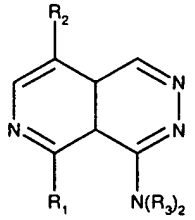

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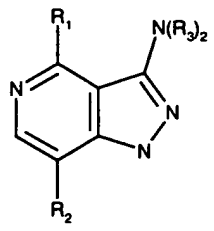

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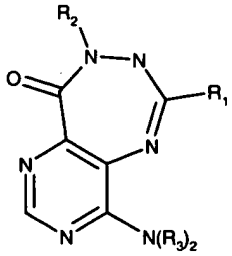

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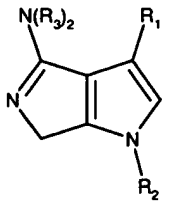

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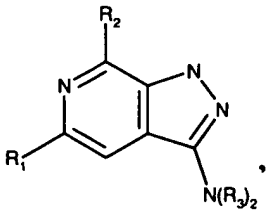

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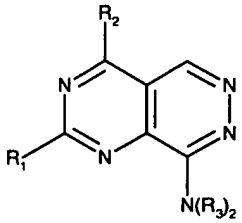

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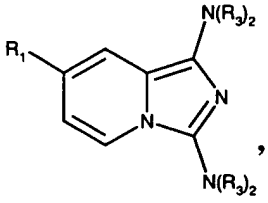

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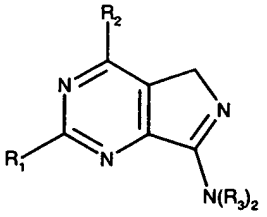

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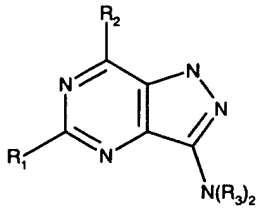

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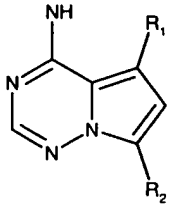

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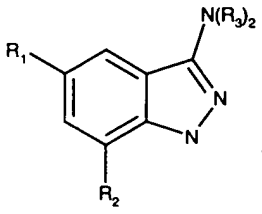

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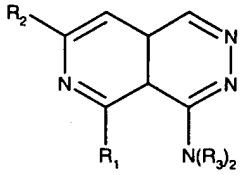

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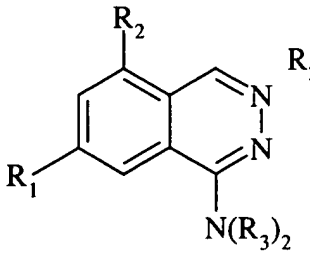

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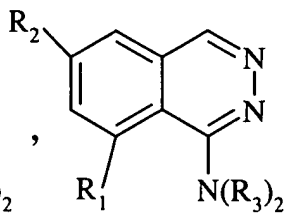

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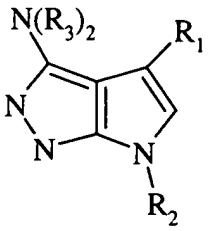

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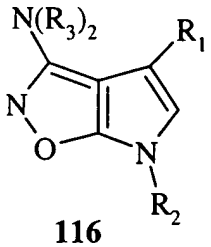

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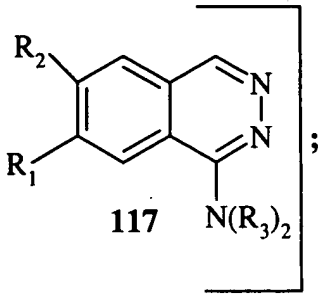

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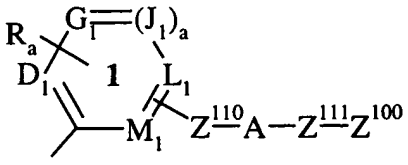
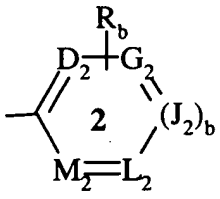
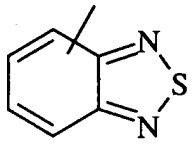
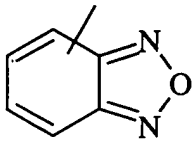
wherein:

R_1 is 

where Z^{100} is  or a group optionally substituted with R_b selected from the group consisting of cycloalkyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl, thienyl, benzoxazolyl, benzothiazolyl,  ,  , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, benzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted -$(CH_2)_n$-cycloalkyl-$(CH_2)_n$-; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN,

OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_1 each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, -NO_2, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z^{105}-C(O)N$(R)_2$, -Z^{105}-N(R)-C(O)-Z^{200}, -Z^{105}-N(R)-S$(O)_2$-Z^{200}, -Z^{105}-N(R)-C(O)-N(R)-Z^{200}, R_c and CH_2OR_c;

where R_c for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, -CH_2-NR_dR_e, -W-$(CH_2)_t$-NR_dR_e, -W-$(CH_2)_t$-Oalkyl, -W-$(CH_2)_t$-S-alkyl, or -W-$(CH_2)_t$-OH;

Z^{105} for each occurrence is independently a covalent bond or $(C_1$-$C_6)$;

Z^{200} for each occurrence is independently a substituted or unsubstituted $(C_1$-$C_6)$, substituted or unsubstituted phenyl or substituted or unsubstituted -$(C_1$-$C_6)$-phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2-alkyl; or R_d, R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring; t for each occurrence is independently an integer from 2 to 6; W for each occurrence is independently a direct bond or O, S, S(O), $S(O)_2$, or NR_f, wherein R_f for each occurrence is independently H or alkyl;

or R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R_3 is hydrogen, hydroxy, substituted or unsubstituted alkyl or substituted or unsubstituted alkoxy;

A is -O-; -S-; -$S(O)_p$-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -N(SO_2R)-; -CH_2O-; -CH_2S-; -CH_2N(R)-; -CH(NR)-; -CH_2N(C(O)R))-;

$-CH_2N(C(O)OR)-$; $-CH_2N(SO_2R)-$; $-CH(NHR)-$; $-CH(NHC(O)R)-$; $-CH(NHSO_2R)-$; $-CH(NHC(O)OR)-$; $-CH(OC(O)R)-$; $-CH(OC(O)NHR)$; $-CH=CH-$; $-C(=NOR)-$; $-C(O)-$; $-CH(OR)-$; $-C(O)N(R)-$; $-N(R)C(O)-$; $-N(R)S(O)_p-$; $-OC(O)N(R)-$; ; $-N(R)-C(O)-(CH_2)_n-N(R)-$, $-N(R)C(O)O-$; $-N(R)-(CH_2)_{n+1}-C(O)-$, $-S(O)_pN(R)-$; $-O-(CR_2)_{n+1}-C(O)-$, $-O-(CR_2)_{n+1}-O-$, $-N(C(O)R)S(O)_p-$; $-N(R)S(O)_pN(R)-$; $-N(R)-C(O)-(CH_2)_n-O-$, $-C(O)N(R)C(O)-$; $-S(O)_pN(R)C(O)-$; $-OS(O)_pN(R)-$; $-N(R)S(O)_pO-$; $-N(R)S(O)_pC(O)-$; $-SO_pN(C(O)R)-$; $-N(R)SO_pN(R)-$; $-C(O)O-$; $-N(R)P(OR_g)O-$; $-N(R)P(OR_g)-$; $-N(R)P(O)(OR_g)O-$; $-N(R)P(O)(OR_g)-$; $-N(C(O)R)P(OR_g)O-$; $-N(C(O)R)P(OR_g)-$; $-N(C(O)R)P(O)(OR_g)O-$, or $-N(C(O)R)P(OR_g)-$;

where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_g for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2;

or in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R_g together form a five- or six-membered heterocyclic ring; or

A is $NRSO_2$ and R, R_a and the nitrogen atom together form a substituted or unsubstituted five or-six-membered heterocyclic ring fused to ring 1;

R_2 is $-Z^{101}-Z^{102}$;

Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted or unsubstituted phenyl group;

Z^{102} is hydrogen, a substituted or unsubstituted alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted, saturated or unsaturated heterocyclic group, or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group;

said substituted heterocyclic or substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, substituted or unsubstituted alkoxy, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido; substituted or unsubstituted amino, oxo, a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more nitrogen atoms, one or more oxygen atoms or a combination thereof;

wherein said nitrogen atoms are independently optionally substituted by a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; or

R_2 is of the formula B-E, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalklylcarbonyl, hydroxy, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylenecarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted azacycloalkyl, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino or substituted or unsubstituted aryl;

a is 1 and D_1, G_1, J_1, L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1, G_1, J_1, L_1 and M_1 are CR_a; or

a is 0, and one of D_1, G_1, L_1 and M_1 is NR_a, one of D_1, G_1, L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;

b is 1 and D_2, G_2, J_2, L_2 and M_2 are each independently selected from the group

consisting of CR_a and N, provided that at least two of D_2, G_2, J_2, L_2 and M_2 are CR_a; or

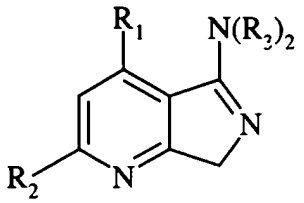
b is 0, and one of D_2, G_2, L_2 and M_2 is NR_a, one of D_2, G_2, L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6.

Appendix B

Pending Claims After Entry Of Amendments

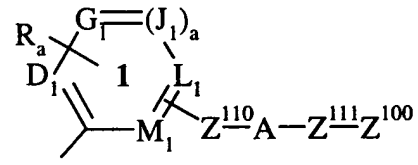
1. (Amended) A compound of Formula (I), the racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof,

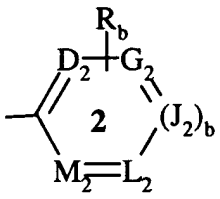
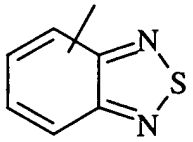
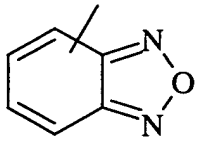


1

,

wherein:

R_1 is 

where Z^{100} is  or a group optionally substituted with R_b selected from the group consisting of cycloalkyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl, thienyl, benzoxazolyl, benzothiazolyl,  ,  , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, benzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted

$-(CH_2)_n$-cycloalkyl-$(CH_2)_n$-; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_1 each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, $-NO_2$, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, $-Z^{105}$-C(O)N$(R)_2$, $-Z^{105}$-N(R)-C(O)-Z^{200}, $-Z^{105}$-N(R)-S$(O)_2$-Z^{200}, $-Z^{105}$-N(R)-C(O)-N(R)-Z^{200}, R_c and CH_2OR_c;

where R_c for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, $-CH_2-NR_dR_e$, $-W-(CH_2)_t-NR_dR_e$, $-W-(CH_2)_t$-Oalkyl, $-W-(CH_2)_t$-S-alkyl, or $-W-(CH_2)_t-OH$;

Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6);

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6), substituted or unsubstituted phenyl or substituted or unsubstituted $-(C_1-C_6)$-phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2-alkyl; or R_d, R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring; t for each occurrence is independently an integer from 2 to 6; W for each occurrence is independently a direct bond or O, S, S(O), $S(O)_2$, or NR_f, wherein R_f for each occurrence is independently H or alkyl;

or R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R_3 is hydroxy, substituted or unsubstituted alkyl or substituted or unsubstituted alkoxy;

A is -O-; -S-; -$S(O)_p$-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -$N(SO_2R)$-;
-CH_2O-; -CH_2S-; -$CH_2N(R)$-; -CH(NR)-; -$CH_2N(C(O)R)$)-;
-$CH_2N(C(O)OR)$-; -$CH_2N(SO_2R)$-; -CH(NHR)-; -CH(NHC(O)R)-;
-$CH(NHSO_2R)$-; -CH(NHC(O)OR)-; -CH(OC(O)R)-; -CH(OC(O)NHR);
-CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-;
-$N(R)S(O)_p$-; -OC(O)N(R)-; ; -N(R)-C(O)-$(CH_2)_n$-N(R)-, -N(R)C(O)O-; -N(R)-
$(CH_2)_{n+1}$-C(O)-, -$S(O)_pN(R)$-; -O-$(CR_2)_{n+1}$-C(O)-, -O-$(CR_2)_{n+1}$-O-,
-$N(C(O)R)S(O)_p$-; -$N(R)S(O)_pN(R)$-; -N(R)-C(O)-$(CH_2)_n$-O-, -C(O)N(R)C(O)-; -
$S(O)_pN(R)C(O)$-; -$OS(O)_pN(R)$-; -$N(R)S(O)_pO$-; -$N(R)S(O)_pC(O)$-; -
$SO_pN(C(O)R)$-; -$N(R)SO_pN(R)$-; -C(O)O-; -$N(R)P(OR_g)O$-; -$N(R)P(OR_g)$-; -
$N(R)P(O)(OR_g)O$-; -$N(R)P(O)(OR_g)$-;
-$N(C(O)R)P(OR_g)O$-; -$N(C(O)R)P(OR_g)$-; -$N(C(O)R)P(O)(OR_g)O$-, or
-$N(C(O)R)P(OR_g)$-;

where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_g for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2;

or in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R_g together form a five- or six-membered heterocyclic ring; or

A is $NRSO_2$ and R, R_a and the nitrogen atom together form a substituted or unsubstituted five or-six-membered heterocyclic ring fused to ring 1;

R_2 is -Z^{101}-Z^{102};

Z^{101} is a covalent bond, -(C_1-C_6)-, -(C_1-C_6)-O-, -(C_1-C_6)-C(O)-, -(C_1-C_6)-C(O)O-, -(C_1-C_6)-C(O)-NH-, -(C_1-C_6)-C(O)-N((C_1-C_6))- or a substituted or unsubstituted phenyl group;

Z^{102} is hydrogen, a substituted or unsubstituted alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted, saturated or unsaturated heterocyclic group, or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group;

said substituted heterocyclic or substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, substituted or unsubstituted alkoxy, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido; substituted or unsubstituted amino, oxo, a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more nitrogen atoms, one or more oxygen atoms or a combination thereof;

wherein said nitrogen atoms are independently optionally substituted by a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; or

R_2 is of the formula B-E, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalklylcarbonyl, hydroxy, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylenecarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted azacycloalkyl, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino or substituted or unsubstituted aryl;

a is 1 and D_1, G_1, J_1, L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1, G_1, J_1, L_1 and M_1 are CR_a; or

a is 0, and one of D_1, G_1, L_1 and M_1 is NR_a, one of D_1, G_1, L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;

b is 1 and D_2, G_2, J_2, L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2, G_2, J_2, L_2 and M_2 are CR_a; or

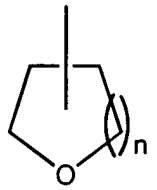
b is 0, and one of D_2, G_2, L_2 and M_2 is NR_a, one of D_2, G_2, L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6.

2. The compound of Claim 1 wherein R_3 is H; R_1 for each occurrence is independently selected from the group consisting of F, Cl, Br, I, CH_3, NO_2, OCF_3, OCH_3, CN, CO_2CH_3, CF_3, -$CH_2NR_dR_e$, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, and substituted or unsubstituted styryl.

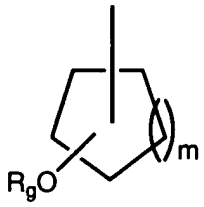
3. The compound of Claim 1 wherein R_3 is H; R_a for each occurrence is independently selected from the group consisting of F, Cl, Br, I, CH_3, NO_2, OCF_3, OCH_3, CN, CO_2CH_3, CF_3, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, and substituted or unsubstituted styryl.

4. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein n is 1, 2 or 3.

5. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

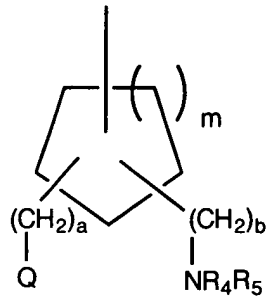


wherein m is 0, 1, 2 or 3 and

R_g is H or $-(CH_2)_pN(R_4)R_5$, wherein p is an integer from 2 to 6 and R_4 and

R_5 are each, independently, H, azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted moiety selected from the group consisting of alkyl, alkoxy, amino, aryl, heteroaryl and heterocycloalkyl group or R_4, R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or heterobicyclic group.

6. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein m is 0, 1, 2 or 3

a and b are each, independently, an integer from 0 to 6;

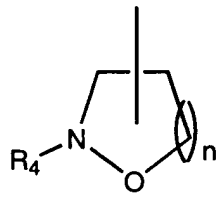
Q is $-OR_6$ or $-NR_4R_5$;

each R_4 and R_5 is, independently, H, azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, amino, aryl, heteroaryl or heterocycloalkyl group or

R_4, R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or heterobicyclic group; and

R_6 is hydrogen or a substituted or unsubstituted alkyl group.

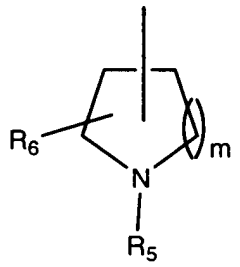
7. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein n is 1, 2 or 3; and

R_4 is H, azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of -C(O)-, $-(CH_2)_q-$, $-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group.

8. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein

m is 0, 1, 2 or 3;

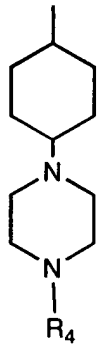
R_5 is H, azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of a covalent bond, -C(O)-, $-(CH_2)_q-$, $-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, $-(CH_2)_qC(O)-$, $-C(O)(CH_2)_q-$ and $-(CH_2)_qS(O)_r-$, where the alkyl portion of $-(CH_2)_q-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, $-(CH_2)_qC(O)-$, $-C(O)(CH_2)_q-$ and $-(CH_2)_qS(O)_r$ is

optionally substituted by a halogen, hydroxy or an alkyl group; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group;

or Y and Z together are a natural or unnatural amino acid, which may be mono- or di-alkylated at the amine nitrogen; and

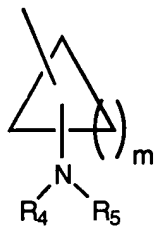
R_6 represents one or more substituents each independently selected from the group consisting of hydrogen, hydroxy, oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heterocyclylcarbonyl, substituted or unsubstituted aminoalkyl and substituted or unsubstituted arylalkyl; provided that the carbon atoms adjacent to the nitrogen atom are not substituted by a hydroxy group.

9. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein R_4 is H, substituted or unsubstituted alkyl, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of -C(O)-, $-(CH_2)_q-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6, and r is 0, 1 or 2; and Z is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl.

10. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



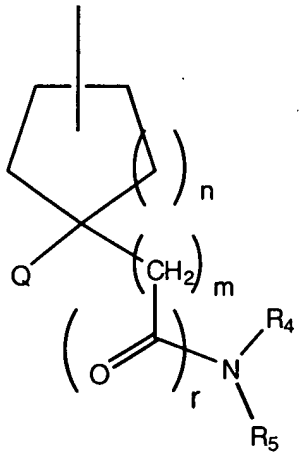
wherein

m is an integer from 1 to 6; and

R_4 and R_5 are each, independently, H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of -C(O)-, $-(CH_2)_q-$, $-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_4, R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterobicyclic group.

11. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein

n is an integer from 0 to 4;

r is 0 and m is an integer from 1 to 6; or

r is 1 and m is an integer from 0 to 6;

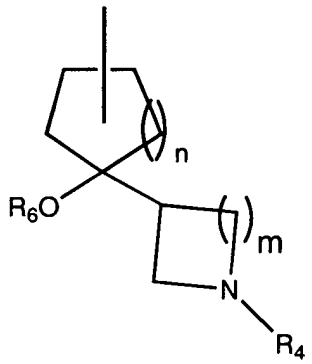
Q is $-OR_6$ or $-NR_4R_5$;

each R_4 and R_5 is, independently, H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$; q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is a substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_4, R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group; and

R_6 is hydrogen or a substituted or unsubstituted alkyl group.

12. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



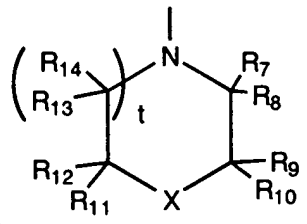
n is an integer from 0 to 4;

m is an integer from 0 to 6;

R_4 is H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and$-(CH_2)_qS(O)_r-$; wherein q is an integer from 0 to 6; and r is 0, 1 or 2; and Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; and

R_6 is hydrogen or a substituted or unsubstituted alkyl group.

13. The compound of Claim 10 wherein R_4, R_5 and the nitrogen atom together form a heterocyclic group of the formula



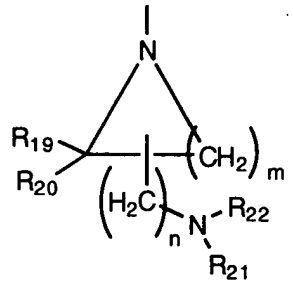
wherein

R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13} and R_{14} are each, independently, lower alkyl or hydrogen; orat least one pair of substituents R_7 and R_8; R_9 and R_{10}; R_{11} and R_{12}; or R_{13} and R_{14} together are an oxygen atom; or at least one of R_7 and R_9 is cyano, $CONHR_{15}$, $COOR_{15}$, CH_2OR_{15} or $CH_2NR_{15}(R_{16})$, wherein R_{15} and R_{16} are each, independently, H, azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, -$(CH_2)_p$-,-$S(O)_2$-, -C(O)O-, -SO_2NH-, -CONH-, $(CH_2)_qO$-, -$(CH_2)_qNH$-, and-$(CH_2)_qS(O)_r$-; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or R_{15}, R_{16} and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or a substituted or unsubstituted heterobicyclic group;

X is O, S, SO, SO_2, CH_2, $CHOR_{17}$ or NR_{17}, wherein R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, -$C(NH)NH_2$, -$C(O)R_{17}$, or -$C(O)OR_{18}$, wherein R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

t is 0 or 1.

14. The compound of Claim 10 wherein R_4, R_5 and the nitrogen atom together form a heterocycle of the formula



wherein

R_{19} and R_{20} are each, independently, hydrogen or lower alkyl; or R_{19} and R_{20} together are an oxygen atom;

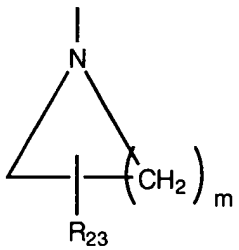
R_{21} and R_{22} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and-$(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_{21}, R_{22} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group;

m is an integer from 1 to 6; and

n is an integer from 0 to 6.

15. The compound of Claim 10 wherein R_4, R_5 and the nitrogen atom together form a heterocyclic group of the formula

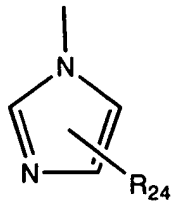


wherein

m is an integer from 1 to 6; and

R_{23} is CH_2OH, NRR', C(O)NRR' or COOR, wherein R and R' are each, independently, hydrogen or substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl.

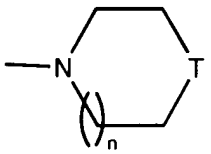
16. The compound of Claim 10 wherein R_4, R_5 and the nitrogen atom together form a heterocyclic group of the formula



wherein R_{24} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl, carboxyl, cyano, $C(O)OR_{25}$, CH_2OR_{25}, $CH_2NR_{26}R_{27}$ or $C(O)NHR_{26}$, wherein R_{25} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterocycloaryl; and R_{26} and R_{27} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected

from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and$-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or R_{26}, R_{27} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group.

17. The compound of Claim 10 wherein at least one of R_4 and R_5 is of the formula Y-Z, wherein Z is of the formula



wherein

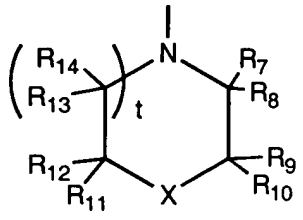
T is C(O), S, SO, SO_2, CHOR or NR, wherein R is hydrogen or a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; and

n is 0, 1 or 2.

18. The compound of Claim 10 wherein at least one of R_4 and R_5 is of the formula Y-Z, wherein Z is of the formula $-N(R_{28})R_{29}$, wherein R_{28} and R_{29} are each, independently, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted alkoxycarbonylalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted cyanoalkyl; or

R_{28} and R_{29}, together with the nitrogen atom, form a five- or six-membered substituted or unsubstituted heterocyclic group.

19. The compound of Claim 11 wherein R_4, R_5 and the nitrogen atom together form a heterocycle of the formula



wherein

R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13} and R_{14} are each, independently, lower alkyl or hydrogen; or at least one pair of substituents R_7 and R_8; R_9 and R_{10}; R_{11} and R_{12}; or R_{13} and R_{14} together are an oxygen atom; or at least one of R_7 and R_9 is cyano, $CONHR_{15}$, $COOR_{15}$, CH_2OR_{15} or $CH_2NR_{15}(R_{16})$, wherein R_{15} and R_{16} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of $-C(O)-$, $-(CH_2)_p-$,$-S(O)_2-$, $-C(O)O-$,

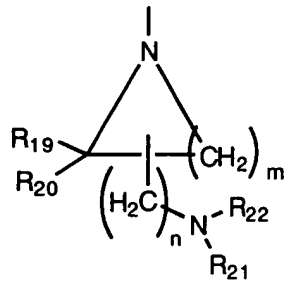
$-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and-$(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl,

substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or R_{15}, R_{16} and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or heterobicyclic group;

X is O, S, SO, SO_2, CH_2, $CHOR_{17}$ or NR_{17}, wherein R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, $-C(NH)NH_2$, $-C(O)R_{18}$, or $-C(O)OR_{18}$, wherein R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

t is 0 or 1.

20. The compound of Claim 11 wherein R_4, R_5 and the nitrogen atom together form a heterocycle of the formula



wherein

R_{19} and R_{20} are each, independently, hydrogen or lower alkyl; or R_{19} and R_{20} together are an oxygen atom;

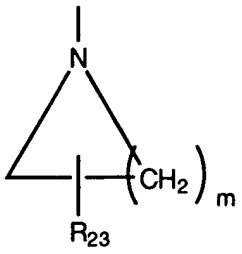
R_{21} and R_{22} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and-$(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_{21}, R_{22} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group;

m is an integer from 1 to 6; and

n is an integer from 0 to 6.

21. The compound of Claim 11 wherein R_4, R_5 and the nitrogen atom together form a heterocyclic group of the formula

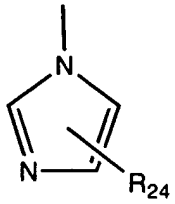


wherein

m is an integer from 1 to 6; and

R_{23} is CH_2OH, NRR', C(O)NRR' or COOR, wherein R is hydrogen or a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group.

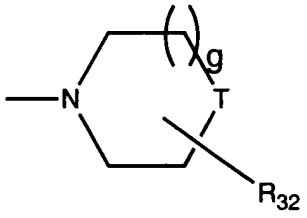
22. The compound of Claim 11 wherein R_4, R_5 and the nitrogen atom together form a heterocyclic group of the formula



wherein R_{24} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl , carboxyl, cyano, $C(O)OR_{25}$, CH_2OR_{25}, $CH_2NR_{26}R_{27}$ or $C(O)NHR_{26}$, wherein R_{25} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterocycloaryl group; and R_{26} and R_{27} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and-$(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or

unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or R_{26}, R_{27} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group.

23. The compound of Claim 11 wherein at least one of R_4 and R_5 is of the formula Y-Z, wherein Z is of the formula



wherein

g is 0 or 1;

T is C(O), O, S, SO, SO_2, CH_2, $CHOR_{17}$ or NR_{17}, wherein R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, $-C(NH)NH_2$, $-C(O)R_{18}$, or $-C(O)OR_{18}$, wherein R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

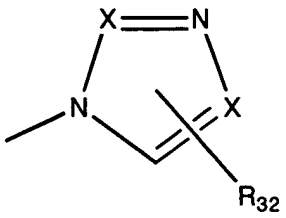
R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl.

24. The compound of Claim 11 wherein at least one of R_4 and R_5 is of the formula Y-Z, wherein Z is of the formula $-N(R_{28})R_{29}$, wherein R_{28} and R_{29} are each, independently, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted alkoxycarbonylalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted cyanoalkyl; or

R_{28} and R_{29}, together with the nitrogen atom, form a five- or six-membered substituted or unsubstituted heterocyclic group.

25. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula $N(R_{30})R_{31}$, wherein R_{30} and R_{31} are each, independently, hydrogen, alkyl, alkoxycarbonyl, alkoxyalkyl, hydroxyalkyl, aminocarbonyl, cyano, alkylcarbonyl or arylalkyl.

26. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula

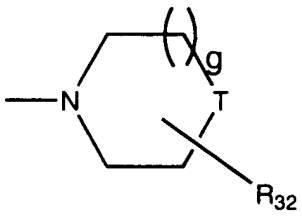


wherein

each X is, independently, CH or N; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

27. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



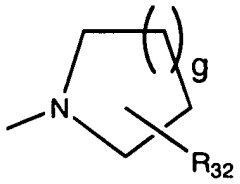
wherein

g is 0 or 1;

T is O, S, SO, SO_2, CH_2, $CHOR_{17}$ or NR_{17}, wherein R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, $C(O)NH_2$, $-C(NH)NH_2$, $-C(O)R_{17}$, or $-C(O)OR_{18}$, wherein R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

28. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula

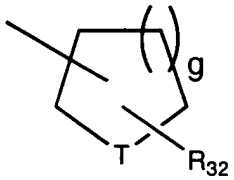


wherein

g is 0, 1 or 2; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

29 The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



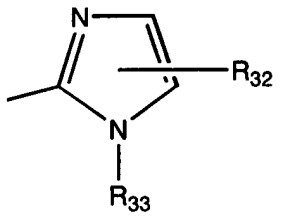
wherein

T is C(O), O, S, SO, SO_2, CH_2, $CHOR_{17}$ or NR_{17}, wherein R_{17} is hydrogen, substituted or unsubstituted alkyl, aryl, arylalkyl, $-C(NH)NH_2$, $-C(O)R_{18}$, or $-C(O)OR_{18}$, wherein R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl;

g is 0 or 1; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

30. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



wherein

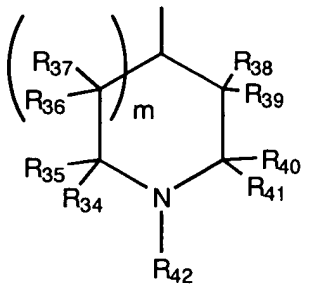
R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl,

substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, alkylcarbonyl , substituted or unsubstituted thioalkoxy or substituted or unsubstituted arylalkyl; and

R_{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl,

substituted or unsubstituted aminocarbonyl, perhaloalkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl.

31. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



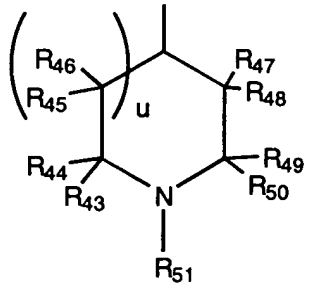
wherein

m is 0 or 1;

R_{34}, R_{35}, R_{36}, R_{37}, R_{38}, R_{39}, R_{40} and R_{41} are each, independently, methyl or hydrogen; or at least one pair of substituents R_{34} and R_{35}; R_{36} and R_{37}; R_{38} and R_{39}; or R_{40} and R_{41} together are an oxygen atom; and

R_{42} is H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and$-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_{42} is of the formula



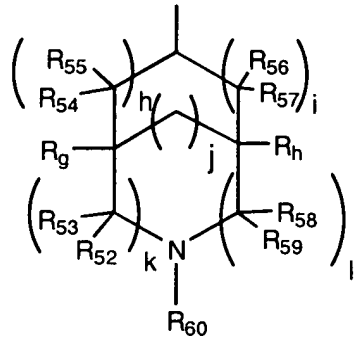
wherein

u is 0 or 1;

R_{43}, R_{44}, R_{45}, R_{46}, R_{47}, R_{48}, R_{49} and R_{50} are each, independently, methyl or hydrogen; or at least one pair of substituents R_{43} and R_{44}; R_{45} and R_{46}; R_{47} and R_{48}; or R_{49} and R_{50} together are an oxygen atom; and

R_{51} is H, substituted or unsubstituted azabicycloalkyl or V-L, wherein V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and$-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl.

32. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

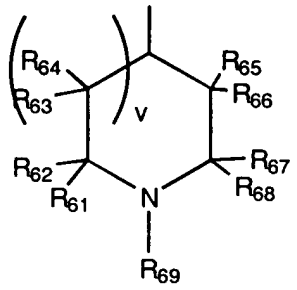


wherein

h, i, j, k and l are independently 0 or 1;

R_{52}, R_{53}, R_{54}, R_{55}, R_{56}, R_{57}, R_{58}, R_{59}, R_g and R_h are each, independently, methyl or hydrogen; or at least one pair of substituents R_{52} and R_{53}; R_{54} and R_{55}; R_{56} and R_{57}; or R_{58} and R_{59} together are an oxygen atom; and

R_{60} is H, substituted or unsubstituted azabicycloalkyl or Y-Z, wherein Y is selected from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and$-(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or R_{60} is of the formula



wherein

v is 0 or 1;

R_{61}, R_{62}, R_{63}, R_{64}, R_{65}, R_{66}, R_{67} and R_{68} are each, independently, lower alkyl or hydrogen; or at least one pair of substituents R_{61} and R_{62}; R_{63} and R_{64}; R_{65} and R_{66}; and R_{67} and R_{68} together are an oxygen atom; and

R_{69} is H, substituted or unsubstituted azabicycloalkyl or V-l, wherein V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$,$-S(O)_2-$, -C(O)O-,

$-SO_2NH-$, -CONH-, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and-$(CH_2)_qS(O)_r-$; wherein p is an integer from 0 to 6, q is an integer from 0 to 6, and r is 0, 1 or 2; and L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl.

33. A method of inhibiting one or more protein kinase activity in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

34. The method of Claim 33 wherein said protein kinase is selected from the group consisting of KDR, FGFR-1, PDGFRβ, PDGFRα, IGF-1R, c-Met, Flt-1, Flt-4, TIE-2, TIE-1, Lck, Src, fyn, Lyn, Blk, hck, fgr and yes.

35. A method of affecting hyperproliferative disorders in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

36. A method of affecting angiogenesis in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

37. The method of Claim 33 wherein the protein kinase is a protein serine/threonine kinase or a protein tyrosine kinase.

38. A method of treating one or more ulcers in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

39. The method of Claim 38 wherein the ulcer or ulcers are caused by a bacterial or fungal infection; or the ulcer or ulcers are Mooren ulcers; or the ulcer or ulcers are a symptom of ulcerative colitis.

40. A method of treating a condition in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient, wherein said condition is an ocular condition, a cardiovascular condition, a cancer, Crow-Fukase (POEMS) syndrome, a diabetic condition, sickle cell anaemia, chronic inflammation, systemic lupus,

glomerulonephritis, synovitis, inflammatory bowel disease, Crohn's disease, glomerulonephritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis, graft rejection, Lyme disease, sepsis, von Hippel Lindau disease, pemphigoid, psoriasis, Paget's disease, polycystic kidney disease, fibrosis, sarcoidosis, cirrhosis, thyroiditis, hyperviscosity syndrome, Osler-Weber-Rendu disease, chronic occlusive pulmonary disease, asthma or edema following burns, trauma, radiation, stroke, hypoxia, ischemia, ovarian hyperstimulation syndrome, preeclampsia, menometrorrhagia, endometriosis, or infection by Herpes simplex, Herpes Zoster, human immunodeficiency virus, parapoxvirus, protozoa or toxoplasmosis.

41. The method of Claim 40 wherein the ocular condition is ocular or macular edema, ocular neovascular disease, scleritis, radial keratotomy, uveitis, vitritis, myopia, optic pits, chronic retinal detachment, post-laser treatment complications, conjunctivitis, Stargardt's disease, Eales disease, retinopathy or macular degeneration.

42. The method of Claim 40 wherein the cardiovascular condition is atherosclerosis, restenosis, ischemia/reperfusion injury, vascular occlusion or carotid obstructive disease.

43. The method of Claim 40 wherein the cancer is a solid tumor, a sarcoma, fibrosarcoma, osteoma, melanoma, retinoblastoma, a rhabdomyosarcoma, glioblastoma, neuroblastoma, teratocarcinoma, an hematopoietic malignancy, Kaposi's sarcoma, Hodgkin's disease, lymphoma, myeloma, leukemia or malignant ascites.

44. The method of Claim 40 wherein the diabetic condition is insulin-dependent diabetes mellitus glaucoma, diabetic retinopathy or microangiopathy.

45. A method of decreasing fertility in a patient, said method comprising the step of administering to the patient an effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolite thereof.

46. The method of Claim 36 wherein the compound or a physiologically acceptable salt, prodrug or biologically active metabolite thereof is administered in an amount effective to promote angiogenesis or vasculogenesis.

47. The method of Claim 34 wherein the protein kinase is Tie-2.

48. The method of Claim 46 wherein the compound of Formula I, or physiologically acceptable salt, prodrug or biologically active metabolite thereof, is administered in combination with a pro-angiogenic growth factor.

49. The method of Claim 48 wherein the pro-angiogenic growth factor is selected from the group consisiting of VEGF, VEGF-B, VEGF-C, VEGF-D, VEGF-E, HGF, FGF-1, FGF-2, derivatives thereof and antiiodotypic antibodies.

50. The method of Claim 46 wherein the patient is suffering from anemia, ischemia, infarct, transplant rejection, a wound, gangrene or necrosis.

51. The method of Claim 33 wherein the protein kinase activity is involved in T cell activation, B cell activation, mast cell degranulation, monocyte activation, the potentiation of an inflammatory response or a combination thereof.

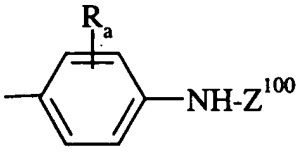
52. A compound according to Claim 1, wherein R_3 is H;

R_2 is $-Z^{101}-Z^{102}$ where Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted phenyl group; and

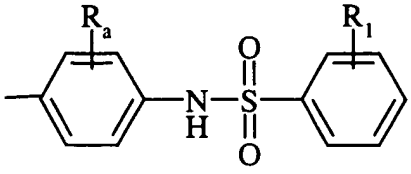
Z^{102} is hydrogen, a substituted or unsubstituted alkyl group or a substituted or unsubstituted, saturated or unsaturated heterocyclic group.

53. A compound according to Claim 52, wherein Z^{101} is selected from the group consisting of $-CH_2-C(O)O-$, $-CH_2-C(O)-$, $-CH_2-C(O)-NH-$, $-CH_2-C(O)-N(Me)-$, $-CH(Me)-C(O)O-$, $-(CH_2)_3-C(O)O-$, $-CH(Me)-C(O)-NH-$, and $-(CH_2)_3-C(O)-NH-$;

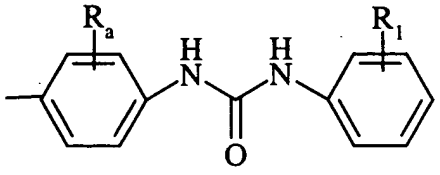
Z^{102} is selected from the group consisting of hydrogen, methyl, ethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, 2-phenyl-2-hydroxyethyl, morpholino, piperazinyl, N-methylpiperazinyl and 2-hydroxymethylpyrrolidinyl.



54. A compound according to Claim 53, wherein R_1 is

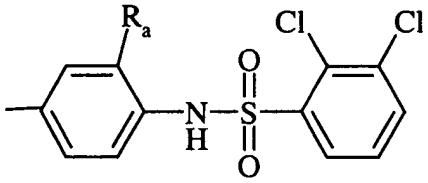


or



where Z^{100} is a substituted or unsubstituted benzoxazolyl or a substituted or unsubstituted benzthiazolyl.

55. A compound according to Claim 8, 9, 10 or 53, wherein R_1 is



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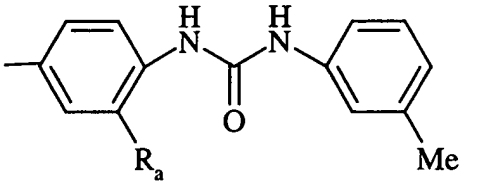

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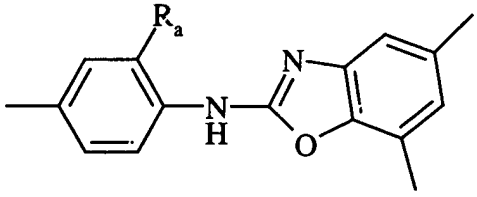
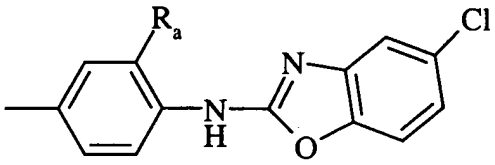
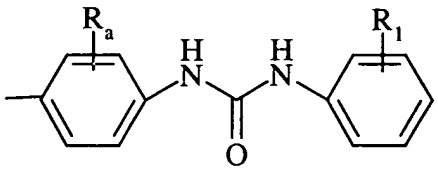


or



where there is only one R_a and it is H or F.

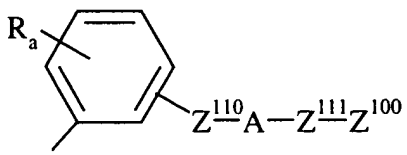
56. A compound according to Claim 52, wherein Z^{101} is a covalent bond; and Z^{102} is an optionally substituted pyridyl.



57. A compound according to Claim 56, wherein R_1 is

58. A compound according to Claim 1, wherein R_3 is H;

R_2 is cyclopentyl; and

R_1 is 

59. A compound according to Claim 58, wherein

Z^{110} is hydrogen;

A is O; and Z^{100} is optionally substituted phenyl, furanyl or thienyl, where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, COOH, NO_2, OMe, -COOMe, OCF_3 and CF_3.

60. A compound according to Claim 58, wherein

Z^{110} is hydrogen;

A is -O-, -O-$(CR_2)_n$-C(O)- or -O-$(CR_2)_n$-O-;

n for each occurrence is 0 to 3;

Z^{100} is an optionally substituted group selected from the group consisting of cyclohexyl, phenyl, tetrahydropyranyl, tetrahydrofuranyl, isoxazolyl and piperidinyl; where Z^{100} is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkoxy, halo, hydroxy and alkoxycarbonyl.

61. A compound according to Claim 58, wherein R^2 is an optionally substituted group selected from the group consisting of cyclobutyl and cyclohexyl.

62. A compound according to Claim 61, wherein R^2 is optionally substituted with one or more substituents selected from the group consisting of hydroxy, alkyl, hydroxyalkyl, carboxyalkyl and phenylalkoxyalkyl.

63. A compound according to Claim 62, wherein R_1 is 4-phenoxyphenyl.

64. A compound according to Claim 6 wherein

m is 2; a is 0; R_6 is H; b is 1 or 2; and R_4 and R_5 are each hydrogen.

65. A compound according to Claim 8, wherein

m is 0, 1 or 2; R_6 is hydrogen; R_5 is H or Y-Z;

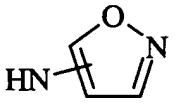
where Y is a covalent bond, -C(O)-, -$(CH_2)_q$O-, -$(CH_2)_q$-, -$(CH_2)_q$C(O)- or -C(O)$(CH_2)_q$-, where the alkyl portion of -$(CH_2)_q$O-, -$(CH_2)_p$-, -$(CH_2)_q$C(O)- and -C(O)$(CH_2)_q$- is optionally substituted by a halogen, hydroxy or an alkyl group; and

Z is hydrogen, alkyl, optionally substituted alkyl, alkoxyalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, or optionally substituted amino.

66. A compound according to Claim 65, wherein

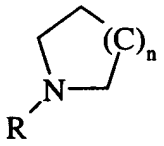
Z is hydrogen, methyl, ethyl, hydroxymethyl, methoxyethyl, N-methyl-piperidinyl, (t-butoxycarbonyl)(hydroxy)-piperidinyl, hydroxypiperidinyl, (hydroxymethyl)piperdinyl,

(hydroxy)(methyl)-piperidinyl, morpholino, (methoxyethyl)piperizinyl, methylpiperizinyl, 4-piperidinylpiperidinyl, imidazolyl, methylimidazolyl, N-methylamino, N,N-dimethylamino, N-isopropylamino, N,N-diethylamino, 2,3-dihydroxypropylamino, 2-hydroxyethylamino, 3-hydroxypropylamino, methoxyethylamino, ethoxycarbonylmethylamino, phenylmethylamino, N-methyl-N-methoxyamino,



, furanylmethylamino, piperidinylethylamino, N-(2-N,N-dimethylaminoethyl)-N-methylamino, 2-N,N-dimethylaminoethylamino, N-methyl-N-(N-methylpiperidin-4-yl)amino, 2-morpholino-ethylamino, 3-morpholino-propylamino, 3-imidazolylpropylamino, or 3-(2-oxopyrrolidinyl)propylamino.

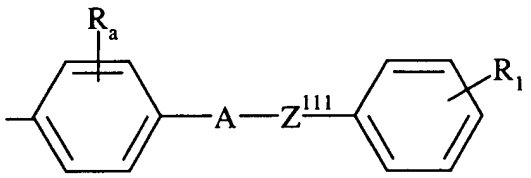
67. A compound according to Claim 8, wherein m is 2; R_5 is Y-Z; Y is -C(O)-; and Z is



where n is 0, 1, 2 or 3.

68. A compound according to Claim 9, wherein

R_4 is hydrogen or methyl;

R_1 is  ;

A is selected from the group consisting of O, -N(R)- and -N(R)C(O)-;

Z^{111} is $-(CH_2)_n$-cycloalkyl-$(CH_2)_n$-;

R is hydrogen or alkyl;

n is 0 to 5;

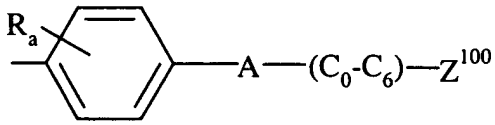
R_a is one or more substituents each independently selected from the group consisting of H, OH, F, Cl, methyl and methoxy; and

R_b is one or more substituents each independently selected from the group consisting of H, CN, F, CF_3, OCF_3, methyl, methoxy and an optionally substituted amino group;

where said amino group is optionally substituted with one or two groups each independently selected from the group consisting of alkyl, alkoxyalkyl, phenyl, substituted phenyl, and optionally substituted heteroaryl.

69. A compound according to Claim 68, wherein R_b is 4-methylphenylthio or 2-pyridinylthio.

70. A compound according to Claim 9, wherein

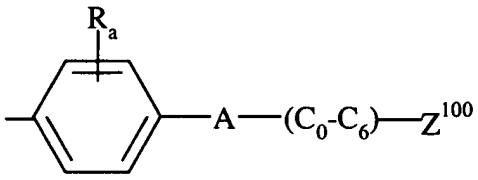


R_1 is

where Z^{100} is selected from the group consisting of benzo[b]thiophene, furanyl and thiophene.

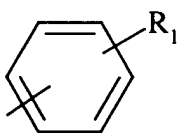
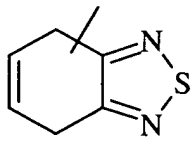
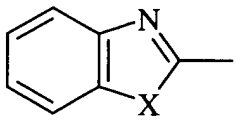
71. A compound according to Claim 9C, wherein R_a is alkoxy; A is -NH-C(O)-; and there is a covalent bond between A and Z^{100}.

72. A compound according to Claims 1, 8 or 9, wherein



R_1 is

A is selected from the group consisting of -N(R)-C(O)-N(R)-, $-(CH_2)_n$-N(R)C(O)N(R)-, -N(R)- and -N(R)-SO_2-; R is hydrogen or alkyl;

Z^{100} is  ,  ,  , pyridinyl, thiazolyl, furanyl, benzofuranyl or oxazolyl;

X is S, O or NR where R for each occurrence is independently H or Me;

R_a is one or more substituents each independently selected from the group consisting of H and F; and

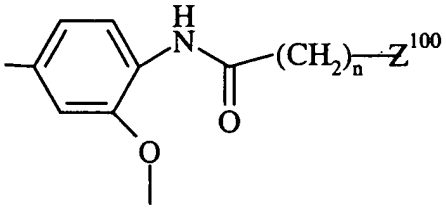
R_b is one or more substituents each independently selected from the group consisting of H, F, Cl, Br, NO_2, CF_3, alkyl, alkoxy and alkoxycarbonyl.

73. A compound according to Claim 72, wherein

R_4 is methyl; m is 1, 2 or 3; R_5 is Y-Z, where Y is -C(O)O-, -C(O)- or -C(O)-$(CH_2)_p$-; and Z is aminoalkyl, N-alkylamino, N,N-dialkylamino or hydroxyalkylaminoalkyl.

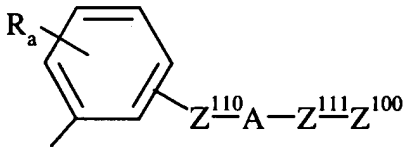
74. A compound according to Claim 9, wherein

R_4 is methyl; R_1 is



where n is 0 to 3; Z^{100} is an optionally substituted group selected from the group consisting of indolyl, indenyl, methylindenyl, methylindolyl, dimethylaminophenyl, phenyl, cyclohexyl and benzofuranyl.

75. A compound according to claim 9, wherein

R_1 is  ;

Z^{100} is an optionally substituted group selected from the group consisting of phenyl, imidazolyl, indolyl, furanyl, benzofuranyl and 2,3-dihydrobenzofuranyl;

where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, Cl, CN, optionally substituted alkyl, -O-(optionally substituted alkyl), -COOH, -Z^{105}-C(O)N$(R)_2$, -Z^{105}-N(R)-C(O)-Z^{200}, -Z^{105}-N(R)-S$(O)_2$-Z^{200}, and -Z^{105}-N(R)-C(O)-N(R)-Z^{200};

Z^{105} is a covalent bond or (C_1-C_6);

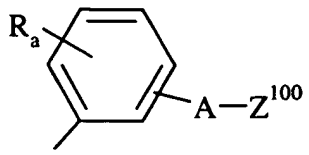
Z^{200} is an optionally substituted group selected from group consisting of (C_1-C_6), phenyl and -(C_1-C_6)-phenyl;

Z^{110} and Z^{111} are each independently a covalent bond or (C_1-C_3) group optionally substituted with alkyl, hydroxy, COOH, CN or phenyl; and

A is O, -N(R)-C(O)-N(R)-, -N(R)-C(O)-O-, -N(R)- or -N(R)-C(O)-, where R is H or alkyl.

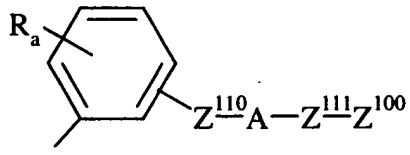
76. A compound according to Claim 75, wherein R_4 is methyl.

77. A compound according to Claim 8, 9 or 10, wherein

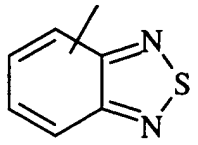
R_1 is  where Z^{100} is an optionally substituted group selected from the group consisting of benzoxazolyl, benzothiazolyl and benzimidazolyl.

78. A compound according to Claim 77, wherein R_4 is methyl; A is -NH-; there is only one R_a and it is H or F; and Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of alkyl, halo, CF_3, and alkoxy.

79. A compound according to Claim 9, wherein

R_1 is  ;

Z^{100} is an optionally substituted group selected from the group consisting of phenyl, pyrrolyl, pyridyl, benzimidazolyl, naphthyl and

 ;

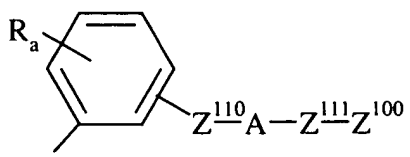
where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, Cl, Br, NO_2, amino, N-alkylamino, N,N-dialkylamino, CN, optionally substituted alkyl, -O-(optionally substituted alkyl) and phenyl;

Z^{110} and Z^{111} for each occurrence is independently (C_0-C_3) optionally substituted with optionally substituted phenyl; and

A is -N(R)-C(O)-N(R)-, -N(R)-S(O)$_2$-, -N(R)-C(O)-, -N(R)- or -N(R)-C(O)-O-.

80. A compound according to Claim 79, wherein R_4 is methyl and there is only one R_a and it is F.

81. A compound according to Claim 9 or 66, wherein

R_1 is  ;

Z^{100} is an optionally substituted group selected from the group consisting of phenyl, isoxazolyl, tetrahydronaphthyl, furanyl, benzofuranyl, pyridyl and indolyl;

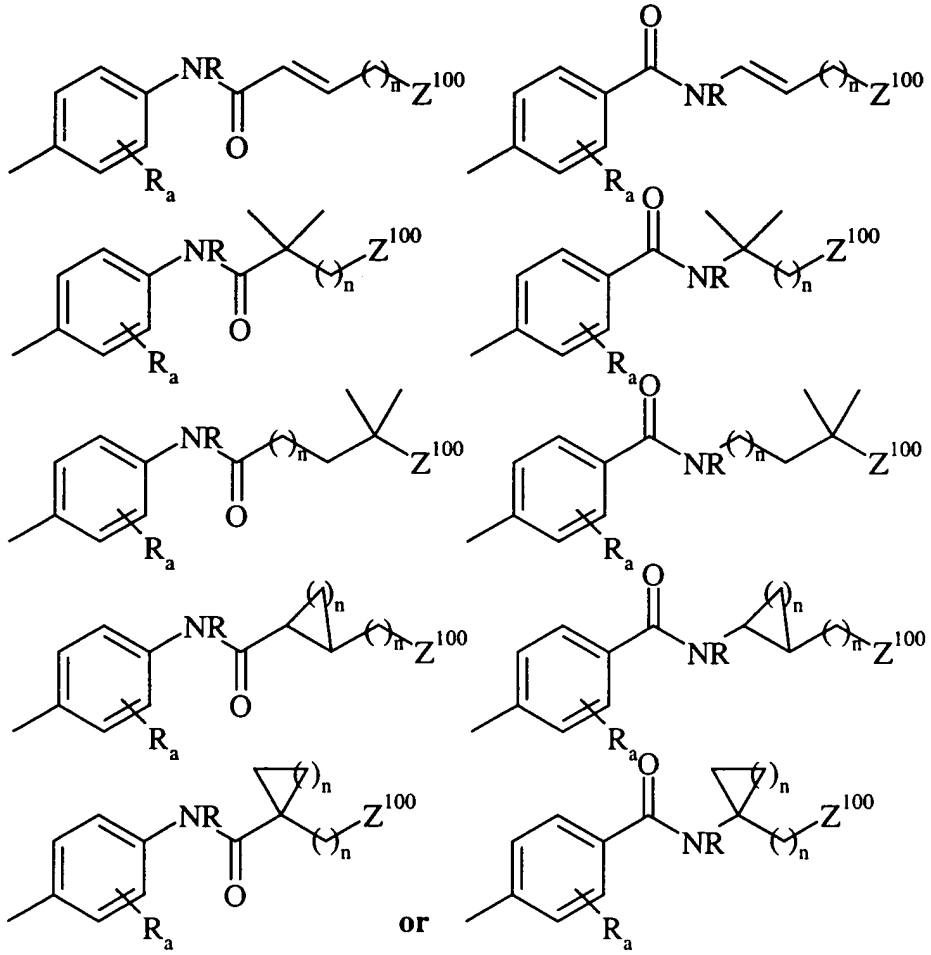
where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, CN, NO_2, -C(O)H, -$CONH_2$, -$NHSO_2CF_3$, optionally substituted alkyl, optionally substituted heteroaryl and -O-(optionally substituted alkyl);

Z^{110} and Z^{111} are each independently optionally substituted (C_0-C_3); and

A is O, -N(R)-C(O)-$(CH_2)_n$-N(R)-, -C(O)-N(R)-, -N(R)-C(O)-O-, -N(R)-C(O)- or -N(R)-.

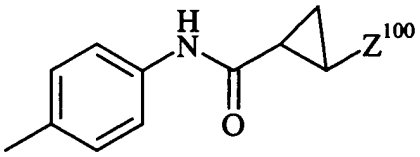
82. A compound according to Claim 81, wherein R_4 is methyl; R_a is H or methoxy; and Z^{110} and Z^{111} are each unsubstituted.

83. A compound according to Claim 9, wherein R_1 is



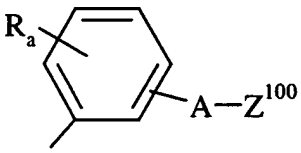
where R is H or lower alkyl and n is for each occurrence is independently 1 to 6.

84. A compound according to Claim 83, wherein R_1 is



85. A compound according to Claim 84, wherein Z^{100} is substituted or unsubstituted phenyl.

86. A compound according to Claim 8, 9 or 10, wherein

R_1 is  where Z^{100} is an optionally substituted group selected from the group consisting of benzoxazolyl, benzothiazolyl and benzimidazolyl.

87. A compound according to Claim 11 wherein n is 2; R_6 is H; m is 1; r is 1; and R_4 and R_5 are each hydrogen.

88. A compound according to claim 64 or 87 wherein R_1 is 4-phenoxyphenyl.